REMARKS

In view of the above amendments and the following remarks, reconsideration of the outstanding office action is respectfully requested. Pursuant to 37 CFR § 1.121, attached as Appendix A is a Version With Markings to Show Changes Made.

Control of plant virus diseases took a major step forward in the last decade when it was shown in 1986 that the tobacco mosaic virus ("TMV") coat protein gene that was expressed in transgenic tobacco conferred resistance to TMV. The concept of pathogen-derived resistance ("PDR"), which states that pathogen genes that are expressed in transgenic plants will confer resistance to infection by the homologous or related pathogens was introduced at about the same time. Since then, numerous reports have confirmed that PDR is a useful strategy for developing transgenic plants that are resistant to many different viruses.

Only eight years after the first reports of PDR, a review of the PDR literature listed the successful development of virus resistant transgenic plants for at least 11 different groups of plant viruses. The vast majority of reports have utilized the coat protein genes of the viruses that are targeted for control. Although the testing of transgenic plants have been largely confined to laboratory and greenhouse experiments, a growing number of reports showed that resistance is effective under field conditions. Two virus resistant crops have been deregulated by APHIS/USDA and, thus, are approved for unrestricted release into the environment in the U.S.A. Squash that are resistant to watermelon mosaic virus 2 and zucchini yellow mosaic potyviruses have been commercialized. Also, a transgenic papaya that is resistant to papaya ringspot virus has been developed. This resistant transgenic papaya was recently deregulated by USDA/APHIS. Deregulation of the transgenic papaya is timely, because Hawaii's papaya industry is being devastated by papaya ringspot virus. Undoubtedly, more crops will be deregulated and commercialized in the near future.

Interestingly, remarkable progress has been made in developing virus resistant transgenic plants despite a poor understanding of the mechanisms involved in the various forms of pathogen-derived resistance. Although most reports deal with the use of coat protein genes to confer resistance, a growing number of reports have shown that viral replicase, movement protein, NIa proteases of potyviruses, and other viral genes are effective. This led to the conclusion that any part of a plant viral genome gives rise to PDR. Furthermore, the viral genes can be effective in the translatable and nontranslatable sense forms, and, less frequently, the antisense forms.

RNA-mediated resistance is the form of PDR where there is clear evidence that viral proteins do not play a role in conferring resistance to the transgenic plant. The first clear cases for RNA-mediated resistance were reported in 1992 for tobacco etch ("TEV") potyvirus, for potato virus Y ("PVY") potyvirus, and for tomato spotted wilt ("TSWV") tospovirus. Others confirmed the occurrence of RNA-mediated resistance with potyviruses, potexviruses, and TSWV and other tospoviruses. More recent work has shown that RNA-mediated resistance also occurs with the comovirus cowpea mosaic virus.

Major advances towards understanding the mechanism(s) of RNA-mediated resistance were made in a series of experiments with TEV and PVY. Using TEV, this group showed that transgenic plants expressing translatable full length coat protein, truncated translatable coat protein, antisense coat protein genes, and nontranslatable coat protein gene had various phenotypic reactions after inoculation with TEV. Transgenic plants displayed resistance, recovery (inoculated plants initially show systemic infection but younger leaves that develop later are symptomless and resistant to the virus), or susceptible phenotypes. Furthermore, they showed that leaves of resistant plants and asymptomatic leaves of recovered plants had relatively low levels of steady state RNA when compared to those in leaves of susceptible plants. However, nuclear run off experiments showed that those plants with low levels of steady state RNA had higher transcription rates of the viral transgene than those plants that were susceptible (and had high steady state RNA levels). To account for these observations, it was proposed "that the resistant state and reduced steady state levels of transgene transcript accumulation are mediated at the cellular level by a cytoplasmic activity that targets specific RNA sequences for inactivation." It was also suggested that the low steady state RNA levels may be due to post-transcriptional gene silencing, a phenomenon that was first proposed by de Carvalho, F., et al., "Suppression of beta-1,3-glucanase Transgene Expression in Homozygous Plants," EMBO J., 11:2595-602 (1992) for the suppression of β-1,3-glucanase transgene in homozygous transgenic plants.

An RNA threshold model was proposed to account for the observations. Basically, the model states that there is a cytoplasmic cellular degradation mechanism that acts to limit the RNA levels in plant cells, and that this mechanism is activated when the transgenic RNA transcript goes above a threshold level. The degradation mechanism is specific for the transcript that goes above the threshold level; and if the transcripts that go above a certain threshold are viral transgenes, the virus resistance state is observed in the plant, because the degradation mechanism also targets, for inactivation, the specific

sequences of the incoming virus. The model also accounts for the 'recovery' of transgenic plants by suggesting that viral RNA from the systemically invading virus triggers the phenomenon in some transgenic plants that have two copies of the transgenes. Plants that had more than three copies of the transgenes caused the threshold level to be surpassed without the invasion of virus. Although the degradation mechanism is not clear, it is proposed that a cellular RNA dependent RNA polymerase ("RdRp") binds to the transcript and produces small fragments of antisense RNA which then bind to other transcripts to form duplexes which are then degraded by nucleases that specifically recognize RNA-RNA duplexes. This degradation mechanism is sequence specific, which accounts for the specificity of RNA-mediated resistance.

Work on PVX confirmed and extended these results. An aberrant RNA model was proposed, where the RNA level is not the sole trigger to activate the cellular degradation mechanism. Instead, aberrant RNA that are produced during the transcription of the transgene play an important part in activating the cytoplasmic cellular mechanism that degrades specific RNA. The production of aberrant RNA may be enhanced by positional affects of the transgene on the chromosome and by methylation of the transgene DNA. The precise nature of the aberrant RNA is not defined, but it may contain a characteristic that makes it a preferred template for the production of antisense RNA by the host encoded RdRp. Thus, the model also proposes that RdRp and antisense molecules are involved in the degradation mechanism. The results of this work confirmed that plants which show low steady state transgene levels have multiple copies of transgenes and that the low steady state RNA and the accompanying resistant state is due to post-transcriptional gene silencing. The term homology-dependent resistance was proposed to describe the resistance in plants that show homology-dependent gene silencing.

Experiments with TSWV tospovirus also showed that resistance in transgenic plants is a consequence of post-transcriptional gene silencing. Pang et al., "Post-Transcriptional Transgene Silencing and Consequent Tospovirus Resistance in Transgenic Lettuce are Affected by Transgene Dosage and Plant Development," Plant Journal, 9:899-09 (1996) showed that post-transcriptional gene silencing in transgenic lettuce expressing the N gene of TSWV was influenced by gene dosage and by the developmental stage of the plant. The effect of developmental stage on post-transcriptional gene silencing of transgenes and their effect on resistance had not been previously shown for transgenic plants expressing viral genes, but had been shown to occur in plants expressing other transgenes. Post-transcriptional gene silencing could also account for the correlation of low steady state level

of N gene RNA in transgenic tobacco showing very high but specific resistance. Pang also reported that post-transcriptional gene silencing occurred with transgenic tobacco expressing the N gene and nonstructural gene of the mRNA (Id.). Interestingly, it was found that tobacco with other parts of the TSWV genome were not resistant. One suggested explanation was that those gene fragments which did not confer resistance may not fit the criteria for inducing post-transcriptional gene silencing. Sijen et al., "RNA-Mediated Virus Resistance: Role of Repeated Transgene and Delineation of Targeted Regions," Plant Cell 8:2227-94 (1996) showed that resistance of transgenic plants expressing the movement protein, replicase, or coat protein were due to post-transcriptional gene silencing. This data also suggested that the 3' region of the movement protein transgene mRNA is the initial target of the silencing mechanism. The present invention is directed to producing improved disease resistant plants.

The objection to the title is respectfully traversed in view of the above amendments.

The objection to the abstract of the disclosure is respectfully traversed in view of the above amendments.

The objection to claims 94, 96-101, 103-109, and 111-121 based on various informalities is respectfully traversed in view of the above amendments.

The rejection of claims 93-121 under 35 U.S.C. § 112 (1st para.) for failure to meet the written description requirement is respectfully traversed.

It is the position of the U.S. Patent and Trademark Office ("PTO") that applicants have not described the claimed compositions in sufficient detail to show that applicants were in possession of the invention as claimed. Applicants disagree.

The present application discloses several types and sources of trait DNAs useful in the present invention (pg. 17, lines 7-33), including the coat protein of papaya ringspot virus ("PRSV") (pg. 17, lines 15-22 and 30-33). Also taught in the specification are DNA molecules that can serve as DNA silencer molecules (pg. 18, lines 21-31), promoters and other regulatory regions that function to allow expression of heterologous DNA in host cells (pg. 21, line 16 to pg. 23, line 8), vectors suitable for expression of the nucleic acids of the invention in host cells (pg. 20, lines 11-34), and expression vector-host systems useful with the nucleic acid molecules of the present application (pg. 21, lines 1-15).

Furthermore, Example 5, 6, and 7 of the present application provide specific details regarding the making of DNA constructs having DNA molecules encoding the coat protein of various viral plant pathogens. Examples 5 and 6 teach that the fusion of a DNA

molecule 110 nucleotides or greater with a silencer provides viral resistance to plants, and Example 7 shows that by combining DNA from multiple viral pathogens in the constructs of the present invention one can impart multiple virus resistance to plants transformed with such constructs.

The present application also teaches that the subject matter of the present application can be used to couple a silencer DNA molecule to fragments of different coat protein encoding genes from different strains of papaya ringspot virus in order to produce a transgenic papaya that is resistant to all papaya ringspot virus strains (pg. 11, line 33 to pg. 12, line 15). Furthermore, the specification teaches that a transgenic papaya that is resistant to papaya ringspot virus was previously developed (pg. 2, line 28 to pg. 3, line 3), and the references cited therein would clearly indicate to one of skill in the art that the nucleotide sequence encoding the coat protein of PRSV was available at the time the present invention was made.

With this information, one of ordinary skill in the art, having read the present application, would understand that at the time the application was filed, applicants were in possession of the invention as claimed.

Therefore, the rejection of claims 93-121 under 35 U.S.C. § 112 (1st para.) for failure to meet the written description requirement should be withdrawn.

The rejection of claims 93-121 under 35 U.S.C. § 112 (1st para.) for lack of enablement is respectfully traversed.

It is the position of the PTO that the present application is enabling for DNA constructs comprising a trait DNA molecule from the tomato spotted wilt and silencer DNA molecules that are the green fluorescent protein and the turnip mosaic potyvirus genes, a method of using such constructs to impart resistance to turnip mosaic potyvirus and tomato spotted wilt virus to a plant, and plants so transformed. However, the specification is deemed non-enabling for DNA constructs where the trait encodes papaya ringspot virus ("PRSV"), methods of using those constructs, and plants and seeds comprising those constructs. Applicants respectfully disagree.

From the passages of the specification referred to in response to the preceding rejection, applicants submit that the claimed invention is fully enabled by the present application. Moreover, as demonstrated below, based on the accompanying Declaration of Dennis Gonsalves Under 37 C.F.R. § 1.132 ("Gonsalves Declaration"), as well as the exhibits referenced therein, the disclosure of the present application would have enabled a skilled scientist to prepare additional DNA constructs having a fragment of a trait DNA from a viral

source, that has at least 110 nucleotides but is less than a full-length cDNA, and a silencer DNA molecule, and to use such constructs to confer a desired trait (e.g., resistance against viral pathogens) to plants by transforming plants with such constructs ("Gonsalves Declaration ¶ 5). In particular, applicants submit that the present application is enabling for DNA constructs having a DNA molecule encoding the coat protein of PRSV and for a method of conferring resistance to PRSV on plants transformed with such DNA constructs (Id.).

Applicant submits that data presented in the present patent application shows that multiple virus resistance can be obtained by transforming plants with a DNA construct that has a silencer DNA (e.g., 726 bp DNA of the green fluorescent protein (GFP) gene, an approximately 400 bp fragment of the nucleoprotein (NP) DNA of tomato spotted wilt virus (TSWV), or the turnip mosaic virus (TurMV) coat protein (CP) DNA) that is linked to short fragments (about 200 bp to 87 bp) of tospovirus (groundnut ringspot virus, impatiens necrotic spot virus, and TSWV) coat protein nucleotide sequence (Example 7) (Gonsalves Declaration ¶ 6). This data also shows that when short DNA segments (200 bp or less) were used in a DNA construct without being linked to a silencer DNA molecule, the construct did not impart resistance to a plant transformed with that construct (Example 5) (Id.). The present application shows that resistance to different viruses can be achieved using the constructs of the present invention, as demonstrated by the resistance imparted to transgenic plants against three tospoviruses, and against a potyvirus and tospovirus (Example 7, with Tables 5-6) (Id.).

Applicant's previous work on developing transgenic papaya for resistance to papaya ringspot virus (PRSV) showed that some strains of PRSV could overcome the resistance in some transgenic papaya lines (Gonsalves Declaration ¶ 7). In particular, the transgenic 'Rainbow' papaya is commercially grown in Hawaii and virtually saved the papaya industry from destruction by PRSV (Id.). However, inoculation experiments have shown that 'Rainbow' is resistant to PRSV strains in Hawaii but is susceptible to a number of PRSV strains from outside of Hawaii (Id.). This differential resistance is largely due to the differences in nucleotide homology between the coat protein genes of different PRSV strains (Id.). In Hawaii, the PRSV strains share at least 97% homology to the PRSV coat protein transgene of 'Rainbow' (Id.). However, some strains, for example, YK from Taiwan and TH from Thailand, share only 89-90% homology to the CP transgene of 'Rainbow' (Id.). Thus, strains of PRSV from Taiwan or Thailand could cause severe damage to the Hawaiian papaya industry if they were introduced to Hawaii (Id.).

Recently, it was also reported from Okinawa that another potyvirus, papaya leaf distortion mosaic virus (PLDMV), causes symptoms similar to PRSV on papaya but is not related to PRSV (Gonsalves Declaration ¶ 8). In fact, the coat protein of PLDMV shares only 49-59% amino acid similarity to the coat protein of PRSV (Id.). Greenhouse inoculations also showed that 'Rainbow' is susceptible to PLDMV. As with various PRSV strains, PLDMV could cause severe damage to the Hawaiian papaya industry if it was introduced to Hawaii (Id.).

In order to develop a Hawaiian transgenic papaya that would be resistant to outside strains of PRSV and simultaneously to PLDMV, DNA constructs in accordance with the present invention were prepared (Gonsalves Declaration ¶ 9). These DNA constructs had a trait DNA that was less than a full-length trait-encoding DNA but containing at least 110 nucleotides, coupled to a DNA silencer molecule, with both the trait and the DNA silencer molecules under the control of a single 35S promoter and single terminator sequence (Id.). Various coding sequences for segments of the PRSV or PLDMV coat protein were incorporated into the DNA constructs (Id.). The constructs were then cloned into a suitable plant expression vector (Id.). Papaya plants were then transformed with the expression vectors containing the DNA constructs and the transgenic papaya were analyzed for resistance to the target viruses (Id.). The data from this work, described in detail herein *infra*, shows the effectiveness of the DNA constructs of the present invention in conferring multiple viral resistance to plants transformed with such constructs (Id.).

Using the techniques described in Example 1 of the present application, basic gene constructs containing the green fluorescent protein (GFP) or one-half of the DNA molecule encoding the nucleocapsid protein (1/2NP) of TSWV under the control of a single promoter and terminator sequence, (i.e., [Promoter]-[GFP]-[DNA segments]-[Terminator] and [Promoter]-[1/2NP] [DNA segments]-[Terminator], respectively) were prepared (Gonsalves Declaration ¶ 10). Various trait DNA segments from a variety of PRSV strains, and/or PLDMV DNA segments, in translatable or non-translatable configurations, and a DNA useful for antibiotic transgene selection following transformation, were inserted into these DNA constructs (Id.).

Immature zygotic embryos extracted from seeds of immature green 'Sunrise' or 'Kapoho' papaya were transformed with expression vectors containing the DNA constructs prepared as described above (Gonsalves Declaration ¶ 11). Transgenic embryos were regenerated in a medium containing the appropriate antibiotic for selection (Id.). Mature somatic embryos surviving selection were transferred to germination medium and

allowed to develop into plantlets with dark green leaves and root initials (Id.). Plants were placed in rooting medium and transferred to the greenhouse (Id.). Transgenic lines from the germination medium were analyzed by PCR to confirm that the viral DNA was in the plantlets (Id.). Northern blots were carried out to detect the level of RNA expressed in transgenic lines, and the copy number of the transgene in the transgenic plants was determined by Southern blot analysis (Id.). Transgenic plants were further cultivated in accordance with conventional procedures so that the DNA construct was present in the resulting plants (Id.). To test viral resistance, plant inoculations with virus were carried out as previously described and systemic symptoms of infection were recorded (Id.). The results are summarized in Table 1 and Table 2 (attached to the Gonsalves Declaration as Exhibits 6 and 7, respectively) (Gonsalves Declaration ¶ 12). The data from Table 1 show resistance against the PRSV strain from Keaau, Hawaii (KE), which is the first virus that the RO plants were tested against (Id.). The data clearly show that a segment of KE DNA (~ 200 nucleotides in length) imparts resistance when linked to the silencer DNA (Id.). This demonstrates that the present patent application teaches constructs and a method for conferring resistance to additional viral plant pathogens such as PRSV (Id.).

Plants that were resistant to KE were then screened for resistance to the other target viruses for which segments of the CP were present in the transgenic papaya (Table 2) (Gonsalves Declaration ¶ 13). In particular, plants were first screened for resistance to KE and, subsequently, the KE-resistant plants were screened for resistance to the other strains of PRSV or to PLDMV (Id.). The data in Table 2 show that applicant's approach provides resistance to various strains of PRSV and to PLDMV (Id.). In particular, two lines (numbers 493 and 494) with the DNA construct pNP-YKT3'PLDMV showed resistance to PRSV strains of KE, TH, and YK, and to PLDMV (Id.). In addition, a transgenic papaya (line number 423) with DNA construct pNP-YKT5'Jap showed resistance to PRSV strains KE, YK, TH, and Jap (Id.). Thus, the approach described by the patent application is enabling for conferring multiple viral resistance, e.g., for PRSV and for PLDMV (Id.).

Furthermore, the nucleotide sequences of many viral plant pathogens are known and available to the skilled scientist (Gonsalves Declaration ¶ 14). For example, a single search request designating nucleotides for "viral plant protein" on the National Center for Biotechnology Information (NCBI) on-line search site generated a list of 288 nucleotide sequences for coat proteins of virus associated with plant pathogenesis that are available on the public (Id.). It is common for research scientists to access publicly available viral genomic sequence information, carry out a BLAST or other type of homology search on that

nucleotide relative to a second sequence of interest, and identify a potentially useful nucleotide sequence from a desired source for a given objective (Id.). Furthermore, at the time the present invention was made the nucleotide sequence encoding the coat protein of PRSV was known (Id.). Thus, it would have been well within the capabilities of a skilled scientist to isolate or synthesize a fragment of 110 nucleotides or more of a desired trait DNA from a viral source, including that of the coat protein of PRSV, for use in a DNA construct. (Id.)

In addition, the present application teaches several types and sources of DNA molecules that can serve as DNA silencer molecules (pg. 18, lines 21-31), promoters and other regulatory regions that function to allow expression of heterologous DNA in host cells (pg. 21, line 16 to pg. 23, line 8), vectors suitable for expression of the nucleic acids of the present invention in host cells (pg. 20, lines 11-34), and expression vector-host systems useful with the nucleic acid molecules of the present application (pg. 21, lines 1-15).

There are a multitude of protocols known to the skilled scientist that teach how to identify and isolate viral DNA, prepare DNA constructs in plant expression vectors, and to transform plants with such expression vectors (Gonsalves Declaration ¶ 15). For example, there are references that specifically disclose methods to obtain and manipulate nucleic acid molecules from plant viruses (Id.). Many other useful references are available which provide specific guidance to the skilled scientist for the transformation, regeneration, and testing of transgenic plants (Id.) For example, Gene Transfer to Plants, Potrykus and Spangenberg, eds., Springer Verlag Press, Berlin (1995) discloses methods for gene transfer to plants using *Agrobacterium*-mediated gene transfer (Parts I and II), protoplast transfer (Part III), biolistic transformation (Part IV), microinjection and fiber-mediated transformation (Part V), and tissue electroporation (Part VI), as well as methods for the analysis of transgenic plants post-transformation (Part VII), the establishment and maintenance of embryogenic cultures (Part VIII), and the use of genetic markers and expression signals in plant transformation (Part IX) (Id.). In addition, the Fitch and Tennant references, cited on pages 2-3 of the present application, specifically teach transforming papaya plants with expression vectors, and regenerating and propagating transgenic papaya plants harboring PRSV transgenes (Id.).

Therefore, it is clear that a skilled scientist having read the present patent application would know how to make additional DNA constructs having a segment of a trait DNA from a viral source, such as the CP of PRSV, that has at least 110 nucleotides but is less than a full-length cDNA, and includes either other trait DNA molecules or a silencer DNA,

under the control of a single promoter sequence and single terminator sequence, and how to use such constructs to prepare expression vectors and host cells, including plant cells, containing those nucleic acid molecule constructs, and, finally, how to prepare transgenic plants to impart a desired trait, e.g., resistance to PRSV, to the transformed plants (Gonsalves Declaration ¶ 16).

Therefore, applicants submit that the present invention, as filed, is fully enabling and that the rejection of claims 93-121 under 35 U.S.C. § 112 (1st para.) for lack of enablement should be withdrawn.

The rejections of claims 93-121 under 35 U.S.C. § 112 (2nd para.) for indefiniteness is respectfully traversed in view of the above amendments, and as noted below.

With regard to the rejection of claims 102, 104-106, 109, and 114, it is the position of the PTO that the terms "trait DNA molecule" and "silencer DNA molecule" are indefinite. Applicants respectfully disagree.

As clearly stated in claim 102, as amended, the DNA construct includes a fragment of trait DNA from a viral source, having at least 110 nucleotides, but is less than a full-length cDNA encoding the trait. The term 'silencer DNA' was fully described in the present application as "virtually any nucleic acid" molecule (pg. 18, lines 21-23). Furthermore, the specification provides examples of the types of nucleic acid molecules that can be used a silencer DNA molecule in the constructs of the present invention (pg. 18, lines 21-31; pg. 40, lines 33-39) as well as providing data demonstrating the efficacy of various silencer DNA molecules in conferring the trait of viral resistance to plants transformed with constructs of the present invention (Example 7). As the claims make clear, the fragment of a trait DNA molecule and the silencer DNA molecule are separate, required elements of the claims. The nature of these components is also readily apparent from the claims. Applicants, therefore, submit that the terms "trait DNA" and "silencer DNA" as described and used in the present application would be clearly understood by one of ordinary skill in the art.

With regard to the rejection of claim 106, the PTO states that it is unclear how the trait DNA can be nontranslatable when the parent claim specifies that the trait DNA encodes a papaya ringspot viral coat protein. Applicants submit that in normal scientific parlance, a DNA molecule is said to encode for a protein when the DNA molecule is capable, under normal circumstances, of encoding mRNA molecules which are translatable to a protein. As amended, claim 106 indicates that the DNA construct has been modified so that the fragment of the trait DNA molecule and the silencer DNA molecule are nontranslatable.

The rejection of claims 93-121 under 35 U.S.C. § 103(a) for obviousness over WO 96/21031 to Tricoli et al. ("Tricoli") is respectfully traversed.

Tricoli teaches a chimeric recombinant DNA molecule comprising a plurality of DNA sequences, each of which has a plant-functional promoter linked to a coding region which encodes a viral coat protein, where the viral DNA sequences are linked in tandem so that they are expressed in virus-susceptible plant cells transformed with the recombinant molecule to impart resistance to the viruses.

It is the PTO's position that it would have been obvious to add an additional trait DNA molecule to the construct taught by Tricoli, in view of Tricoli's success in obtaining plants with resistance to multiple viruses, and thus obtain the DNA construct of the present application. Applicants respectfully disagree.

A proper *prima facie* showing of obviousness requires that the prior art reference must teach or suggest every limitation of the claimed invention. *In re Wilson*, 424 F.2d 1382, 1385, 165 USPQ 494, 496 (CCPA 1970). This is not the case with regard to Tricoli. Tricoli teaches a chimeric recombinant DNA molecule comprising a plurality of DNA sequences, each of which has a plant-functional promoter linked to a coding region which encodes a viral coat protein. The viral DNA sequences, each with its own promoter, are linked in tandem so that they are expressed in virus-susceptible plant cells transformed with the chimeric recombinant DNA molecule to impart resistance to the viruses.

The PTO has apparently interpreted Tricoli as preparing plant expression constructs having more then one viral coat protein-encoding DNA under the control of a single promoter. The PTO's interpretation appears to be based on the preparation by Tricoli of a plant expressible fusion gene consisting of the WMV2 coat protein and the NH_3-terminal portion of the cucumber mosaic virus ("CMV") coat protein gene (pg. 22, lines 15-28). However, the NH_3-terminal portion of the CMV gene used by Tricoli is a 70 nucleotide untranslated region of the CMV gene, which Tricoli uses in plant expression cassettes as an enhancer for translation, i.e., a 5' regulatory region. This is clearly described in Slightom, J.L., "Custom Polymerase-Chain Reaction Engineering of a Plant Expression Vector," Gene 100:251-255, (1991) ("Slightom") (at Abstract; pg. 251; and 252, 1st full para.) (attached hereto as Appendix B), which is cited by Tricoli at pg. 22, lines 23-24. The structure and function of the CMV-CP DNA segment in the construct is also made clear in Tricoli at pg. 23, lines 21-26. The CMV-CP/WMV2 construct is then further modified by the addition of the CaMV 35S plant promoter and polyadenylation signal to produce a plant expressible coat protein cassette, as described in Slightom (Tricoli at pg. 22, lines 20-24). Tricoli teaches that

the expression cassettes for zucchini yellow mosaic virus (ZYMV), cucumber mosaic virus (CMV), and squash mosaic virus (SQMV) coat protein are all prepared in the manner taught by Slightom. Each of the coat protein expression constructs thus prepared is defined by Tricoli as a single coat protein cassette (see pg. 24, line 11). To make multiple coat protein-expressing constructs, Tricoli takes single coat protein cassettes, each containing one full-length cDNA for a viral coat protein, coupled to the 70 nucleotide 5' untranslated enhancer region of the CMV Cp, a CaMV 35S promoter, and 35S terminator, and places the cassettes together in various combinations in a vector in order to obtain binary plasmids (see pg. 24, line 10 to pg. 26, line 9). Thus, Tricoli does not teach or suggest "[a] DNA construct comprising: a plurality of fragments of trait DNA molecules at least some of which have a length that is independently insufficient to impart that trait to plants transformed with that fragment of a trait DNA molecule, wherein the fragments of trait DNA molecules are at least 110 nucleotides in length but are less than a full-length DNA," and that has "a single promoter sequence which effects transcription of the plurality of fragments of trait DNA molecules; and a single termination sequence which ends transcription of the plurality of fragments of trait DNA molecules", as set forth in claim 93. Nor does Tricoli teach or suggest ":[a] DNA construct comprising: a fragment of a trait DNA molecule which has a length that is insufficient to independently impart a desired trait to plants transformed with said fragment of a trait DNA molecule, wherein the fragment of a trait molecule is derived from a DNA molecule encoding a papaya ringspot virus coat protein and is at least 110 nucleotides in length;" and that has "a silencer DNA molecule effective to achieve post-transcriptional gene silencing of said fragment of a trait DNA molecule" with "a single promoter sequence which effects transcription of the fragment of a trait DNA molecule and the silencer DNA molecule; and a single termination sequence which ends transcription of the fragment of a trait DNA molecule and the silencer DNA molecule." Instead, the expression vectors of Tricoli are constructed so that each viral protein is a full length DNA molecule encoding the viral CP of choice, and each individual viral CP DNA molecule is under the control of a promoter and a termination sequence. There is no suggestion or motivation in Tricoli to place multiple coding sequences under the control of a single promoter sequence and a single terminator sequence, as in the claimed invention. Furthermore, there is no suggestion in Tricoli that anything less than a full-length DNA encoding the desired trait would be effective to confer resistance to a plant transformed with such a construct. Therefore, Tricoli does not teach or suggest every limitation of the claimed

invention. In addition, even if one had added additional DNA molecules to the construct of Tricoli, it would not have resulted in the DNA construct of the present invention.

Accordingly, applicants submit that the rejection of claims 93-121 under 35 U.S.C. §103(a) for obviousness over Tricoli is improper and should be withdrawn.

The provisional rejection of claims 93-121 under the judicially created doctrine of obviousness-type double patenting as unpatentable over claims 5, 12, and 36 of copending U.S. Patent Application Serial No. 09/025,635 is respectfully traversed in view of applicants' submission of the accompanying terminal disclaimer.

In view of all of the foregoing, applicants submit that this case is in condition for allowance and such allowance is earnestly solicited.

Respectfully submitted,

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June 9, 2003 Date	Jo Ann Whalen